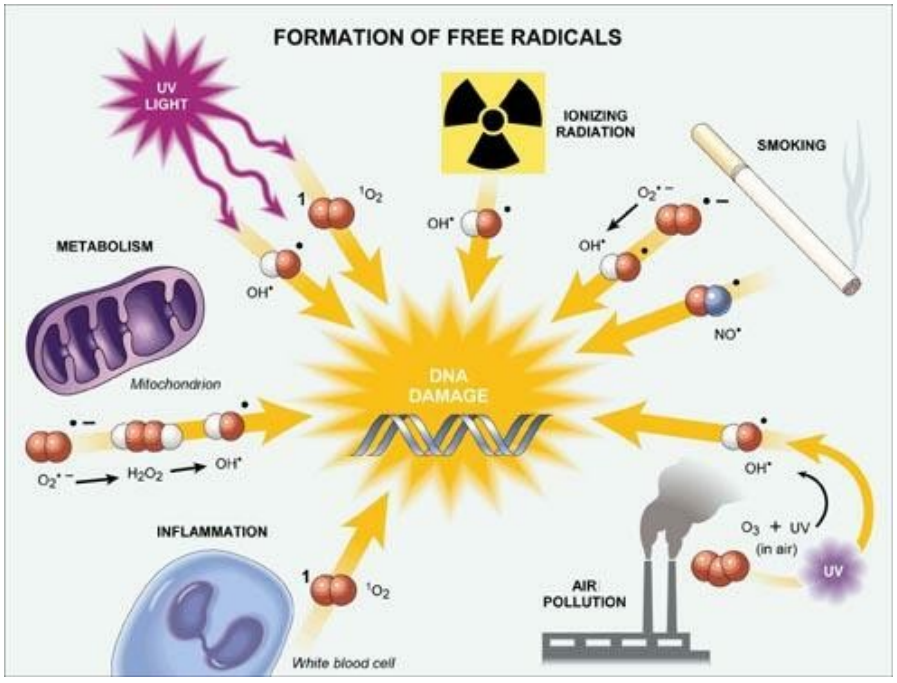
Radiation Hormesis

Introduction

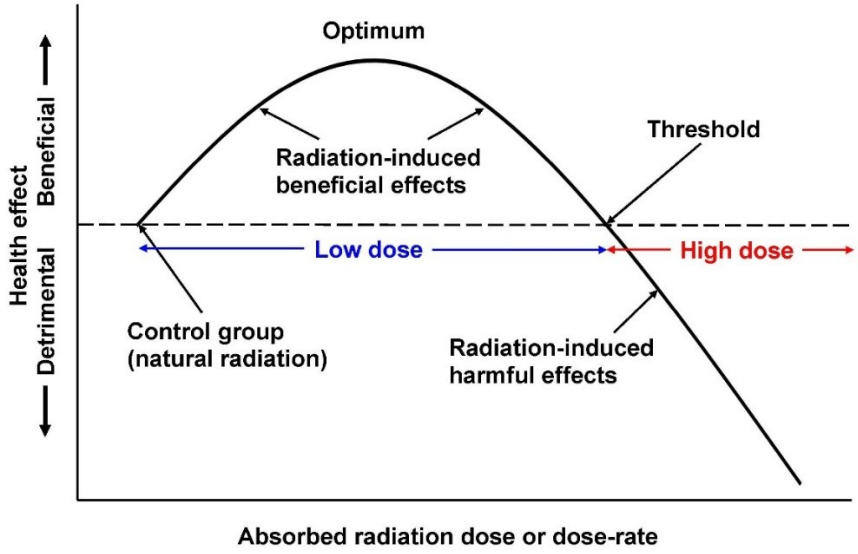
Biological adaptive protection mechanisms have been critical to the survival of humans since life first appeared on Earth. Hormesis is an innate biological ability that enhances survival and biological performance across a wide range of activities via *upregulation* of adaptive response mechanisms following exposure to low levels of potentially harmful stressor agents. Low-dose enhancement is a consequence of *genomic stress adaptation*, without which humans would not exist today given all the genomic stresses encountered throughout life.

Ionizing Radiation-Induced DNA Damage and Hormesis

Aerobic metabolism, necessary for complex multicellular life and essential life functions, is the primary stressor agent causing DNA damage via production of reactive oxygen species (ROS). Ionizing radiation is one of numerous other stressor agents that can also damage DNA by producing ROS, as illustrated in the following graphic.



Humans have forever been exposed to ionizing radiation throughout life, yet have not perished even though radiation levels were much higher when humans first inhabited the planet. Low radiation doses associated with natural background radiation exposure promote hormesis as illustrated in the generalized hormesis curve below.



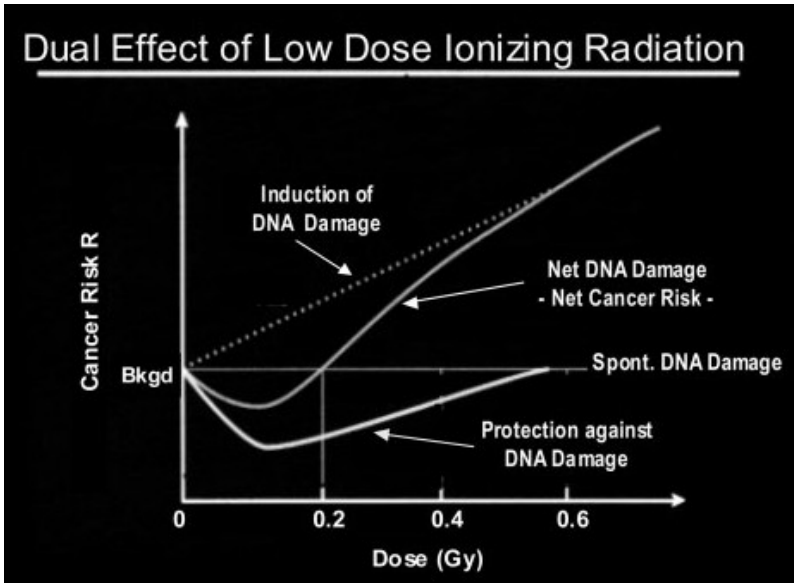
The curve illustrates a range of absorbed radiation doses (or dose-rates) comprising a hormetic zone that benefits an organism by uprating its biological adaptive protective mechanisms. The maximum beneficial response corresponds to the optimum radiation dose and the threshold dose is where the biological response transitions from a beneficial effect to an adverse effect.

Hormesis repairs more than 99.9% of DNA damage by way of six adaptive response mechanisms that inhibit cancer occurrence and extend human longevity:

- enhanced production of antioxidant enzymes
- enhanced production of DNA repair enzymes
- decelerated mitosis (provides DNA repair enzymes time to accomplish their function)
- induced apoptosis (destroys unrepaired cells)
- bystander effects (neighboring undamaged cells trade chemical messengers to enhance apoptosis in cells with unrepaired DNA)
- enhanced immune system surveillance and removal of remaining unrepaired cells

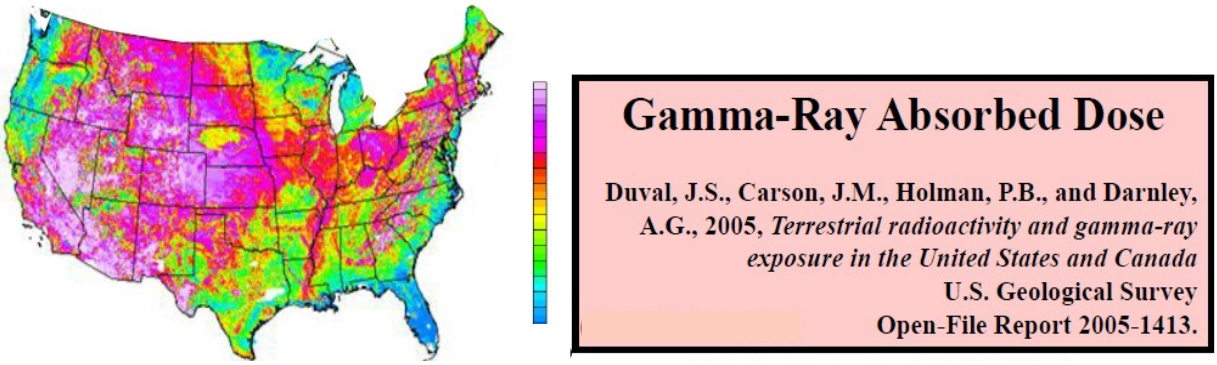
Although large acute doses of ionizing radiation can induce cancer, small doses reduce cancer mortality in both animals and humans. Hormesis is applicable to the physiological effects of acute low Linear Energy Transfer (LET) radiation exposures in the range of 0 to 0.5 Gy of total absorbed dose (see graphic below). The body's hormetic response is dependent on dose-rate as well as total dose.

The probability of radiation-induced adaptive protection measurably outweighs the probability of damage from acute whole-body doses below 0.2 Gy of low LET radiation as shown in the graphic below.[1]



U.S. Background Radiation Exposure and Cancer Mortality

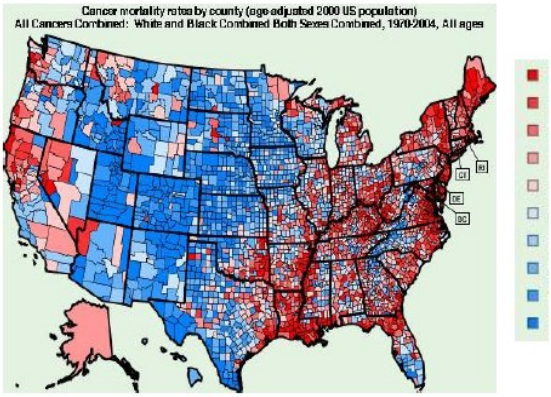
The first two maps below show parts of the western U.S. as having some of the highest natural background gamma-ray and cosmic-ray radiation, respectively, while the third map (from a no longer existing U.S. government website) shows those same regions as also having some of the lowest cancer mortality rates.


Gamma-Ray Absorbed Dose
Duval, J.S., Carson, J.M., Holman, P.B., and Darnley, A.G., 2005, Terrestrial radioactivity and gamma-ray exposure in the United States and Canada
U.S. Geological Survey
Open-File Report 2005-1413.

Cosmic-ray Exposure

(calculated from the topography)

U.S. Geological Survey
Open-File Report 2005-1413.


Cancer mortality rates by county (age-adjusted 2000 US population)
All Cancers Combined: White and Black Combined Both Sexes Combined, 1970-2004, All ages

Cancer Mortality Rates by County

All Cancers, etc.…
1970-2004
Deaths per 100,000 person-years

Likewise, while parts of the eastern and southeastern U.S. have some of the lowest gamma-ray and cosmic-ray exposures, these regions also have some of the highest cancer mortality rates. While these correlations are not proof of cause and effect, the observations are entirely consistent with low-dose ionizing radiation being an hormesis-inducing stressor agent.

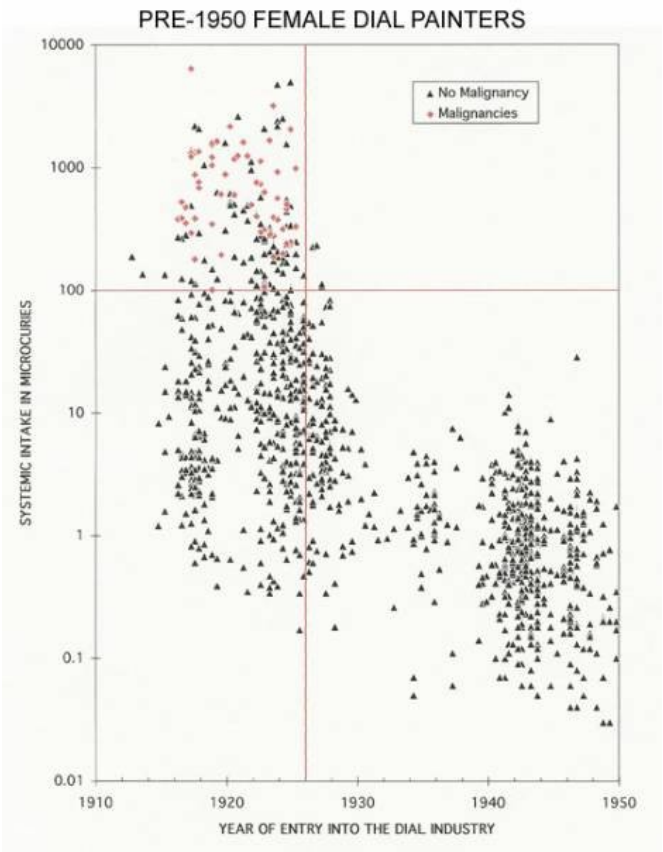
Data that supports the cause and effect of radiation hormesis has been obtained from several radiation studies.

Radium Dial Painters

Selective reporting of information has led to the widespread belief that most radium dial painters died from radiation-induced cancer, which is not true. Beginning around 1915, many women were employed in well-paying jobs to paint hands and faces of clocks and watches with radium paint. At that time little was known about ionizing radiation or its effects. These women ingested radium-226 (Ra-226) from twirling the tip of the paintbrush between their lips to make a fine point. After 5 years, 18 female radium dial painters had developed necrosis (cell death) of jaw bones and pernicious anemia from chronic exposure to internal high-LET alpha particle radiation while others developed possible osteosarcomas (bone tumors).[2]

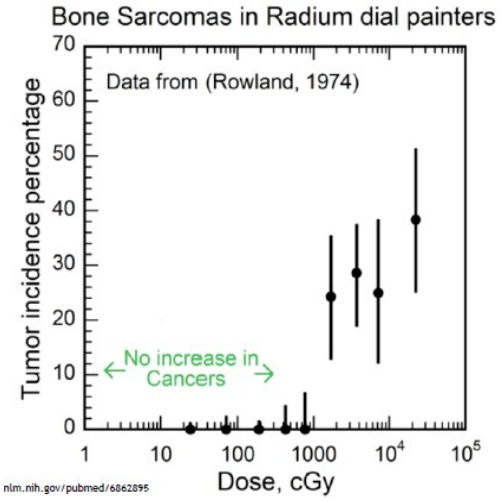
In 1981 Dr. Robley Evans of MIT reported that in thousands of radium dial painter cases worldwide there were no occurrences of bone cancer or nasal carcinoma in individuals who ingested less than 250 microcuries of Ra-226.[3]

In 1997 Dr. Robert Rowland presented radium-induced cancer data based on very reliable body count measurements for 2,383 female dial painters.[4] The scatterplot below shows the radium intake in microcuries for each of these women based on when they entered the workforce.[5] All 64 occurrences of bone sarcoma (cancer tumor) occurred among 264 women who ingested more than 100 microcuries of Ra-226, which resulted in an internal absorbed dose of more than 10 Gy. No sarcomas appeared in the 2,119 women who ingested less than 100 microcuries of Ra-226.



This data indicates the existence of a threshold dose for biological harm from chronic internal exposure to Ra-226 radiation of 10 Gy. This dose, accumulated over a 10-year period, represents an average chronic dose-rate threshold of 0.11 mGy per hour.

A chronic internal radiation dose threshold of 10 Gy (1000 cGy) is also evident in the graph below, which shows the percentage of bone sarcoma incidence in radium dial painters as a function of internal dose.[6]



A 30-year follow-up of 1175 low-dose radium dial painters showed a lower cancer *incidence* than the general population and a longer life span.[2] There was no observed excess *incidence* of bone cancers when the total chronic absorbed dose was below 10 Gy. Except for breast cancer, other cancer *mortality* rates showed no change from the general population and leukemia *mortality* in U.S. female radium dial painters was much lower than expected.

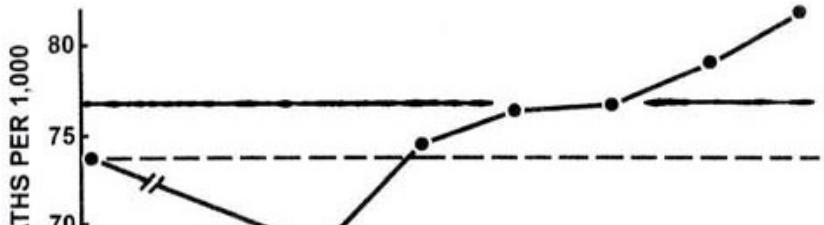
So, this data supports hormesis for chronic internal Ra-226 exposures with an upper dose threshold of 10 Gy (upper dose-rate threshold of 0.11 mGy/hr).

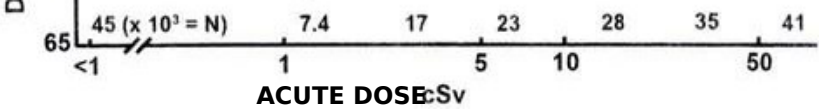
Japanese Atomic Bomb Survivors

Conclusions about the effects of acute radiation exposure are generally based on data from Japanese atomic bomb survivors. There were about 200,000 fatalities from the atomic bombs that were dropped on Hiroshima and Nagasaki in August 1945. The vast majority died from the thermal blast (fireball) and the subsequent shockwave that destroyed occupied buildings, while less than 10% died from acute radiation syndrome.

86,520 survivors who were subjected to high acute low-LET radiation doses have been extensively studied by the Radiation Effects Research Foundation (RERF).[7] Subsequent survivor cancer mortality was compared with people located 3-10 km from ground zero (in-the-city cohort) who received some radiation from the bombs as well as residual radiation from entering the area inside the 3 km radius, and with unexposed people in villages northwest of Hiroshima (out-of-city cohort).

The graph below shows that the cancer mortality rate for the 7,430 survivors receiving 1-1.9 cSv exposure was less than for both control populations, while the 28,423 survivors receiving less than 20 cSv had essentially the same mortality rate as the out-of-city control population.[8]





(Numbers above abscissa indicate thousands of people included in each point; i.e. the number receiving a dose ≤ *x*. **Dashed and solid horizontal lines represent mortality rates for "in-the-city" and "out-of-city" control populations, respectively.**)

This data clearly indicates an hormesis effect for acute doses below 3 cSv and a threshold for increased cancer risk at about 20 cSv (or 200 mGy for low-LET radiation).

Later studies confirmed a reduced cancer *mortality*, reduced leukemia *mortality* and increased average lifespan of Japanese atomic bomb survivors.[9,10,11,12] Likewise, fewer genetic abnormalities were observed in Japanese babies whose mothers received low-LET radiation doses less than 20 cSv.[13]

Nuclear Shipyard Worker Study

Completed in 1987, the Nuclear Shipyard Workers Study[14] was one of the largest and most thorough studies of the effects of low-level (chronic) radiation on nuclear industry workers. The 10-year study matched 39,004 nuclear workers with 33,352 non-nuclear workers in a naval shipyard.

The nuclear workers in the study were exposed to external cobalt-60 (Co-60) radiation produced by neutron activation of Co-59 in nuclear reactor coolant system pipes and valves. These workers were divided into two groups based on their radiation exposures. Members of the high-dose group received a cumulative dose effective (summation of individual irradiated tissue and organ doses) greater than 500 mrem (5 mGy of low-LET radiation), while the cumulative dose effective for the low-dose group was less than 500 mrem.

Mortality rates of 76% and 81% of that for the non-nuclear workers in the control group were found for the high- and low-dose groups, respectively, indicating a likely beneficial effect from their radiation exposures.

Other Nuclear Worker Studies

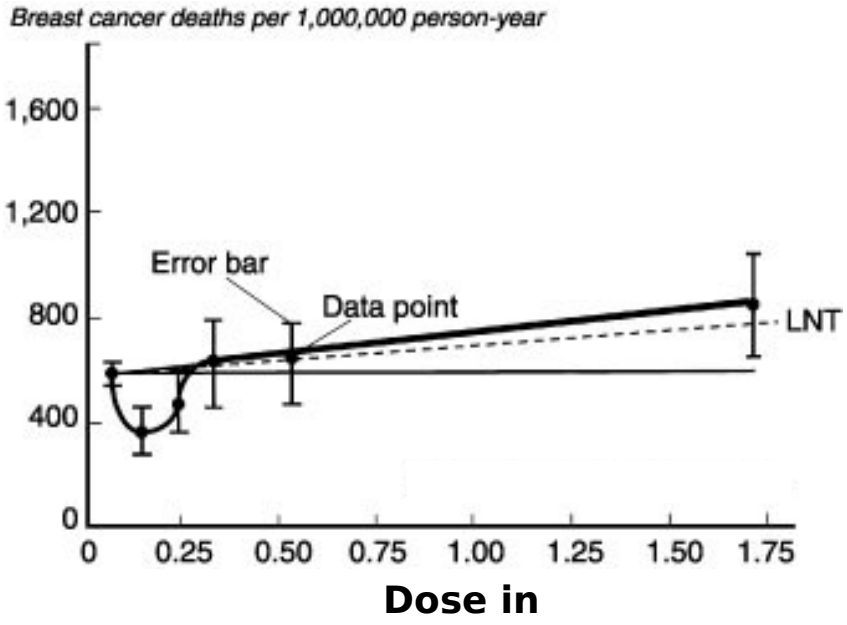
Studies involving more than7 million person-years of experience with nuclear workers provided consistent and convincing evidence that low doses of external ionizing radiation decrease total cancer *mortality* rates.[15,16,17,18] The table below provides summary data from some of those studies, clearly indicating an hormesis effect for low-dose radiation exposures.

		Control/ Exposed		
Study[a]	Dose[b] (mSv)	Population (x 10^3)	Deaths (per 10^3)	Exposed Pop. Deaths as % of Control Pop. Deaths
1	7	21/4	22.0/2.0	9.1
2	20	4.7/3.3	23.7/20.3	85.7
3	66	20.6/15.3	34.8/20.8	59.8
4	25	11.4/2.9	20.5/17.7	86.3

Table notes:
a. 1 – Nuclear Fuel Cycle Workers
2 – Atomic Energy of Canada Limited Workers
3 – Hanford/Oak Ridge/Rocky Flats Workers
4 – Los Alamos Workers (incl. Pu exposure)
b. Estimated lifetime dose per exposed person

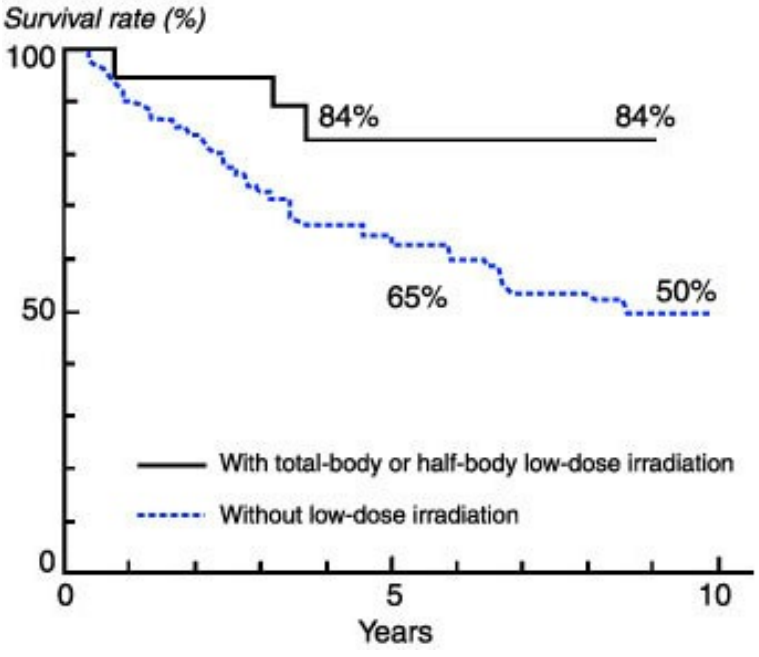
Canadian Fluoroscopy Study

A 1989 study of breast cancer incidence in Canadian women being treated for tuberculosis with high fluoroscopy (x-ray) doses revealed that acute exposures of less than 30 cGy (300 mGy) showed a statistically significant reduction in breast cancer (graph below).[19]



Non-Hodgkin's Lymphoma Trial

A 9-year clinical trial on non-Hodgkin's lymphoma patients receiving low-dose radiation treatments confirmed that the low-dose radiation group substantially outlived the control group at 5 years and 10 years.[20] The trial consisted of 23 low-dose radiation patients and 94 control (unirradiated) patients with similar histological tumor grades. The graph below shows the survival rate of low-dose radiation patients was 84 percent, compared with 50 percent survival of control patients at 10 years.[21]



Taiwan Apartment Dwellers

20,000 tons of Co-60 contaminated steel was used in the construction of 200 apartment buildings in Taipei City, Taiwan in 1983. 10,000 occupants of these apartments received an average collective dose of 400 mSv between 1983 and 2002. The average dose in the first year was approximately 78 mSv, with individual doses ranging from 18 to 525 mSv.

The cancer *mortality* rate for the exposed apartment dwellers was assessed to be 3.5 per 100,000 person- years.[22,23] The average spontaneous cancer death rate for the general Taiwan population over the same 20-year period was 116 deaths per 100,000 person-years.[22,24] The births with congenital heart malformations was assessed to be 1.5 cases per 1,000 children for the apartment population.[22,23] Based on partial official statistics and hospital experience, the general population rate for congenital heart malformations was 23 cases per 1,000 children.[22,24]

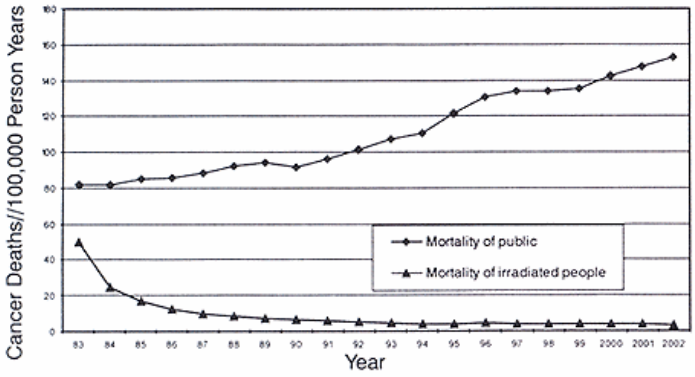


Figure 1. Cancer Mortality of the General Population and of the Exposed Population

Conclusion

Low-dose radiation acts as an hormesis-induced stressor agent.

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